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OFFICIAL

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Executive Director Antisense Lead Identification
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EDUCATION:

University of California, Berkeley, California
Ph.D in Chemistry, 1976

Carleton College, Northfield, Minnesota
B.A. in Mathematics, summa cum laude, 1972

AWARDS:

Damon Runyon-Walter Winchell Cancer Fund
Fellow (1976-1978)
California Regents Fellow (1974-1976)
NSF Graduate Trainee (1972-1973)

OTHER:

Served on Genome Study Section NIH 1997-2002,
Chair 2000-2002

EXPERIENCE:

ISIS

Pharmaceuticals
San Diego
1990-present

Current title: *Executive Director Antisense Lead Identification*

- Determination of microRNA function in mammals. Includes computational identification of miRNAs and miRNA targets. Functional genomics to characterize miRNA biology and identify therapeutic applications of modulation of miRNA activity.
- Use of antisense oligonucleotides for functional genomics of novel targets. Includes: Computational genomics to characterize target RNAs and their variants, rapid throughput screening to identify active antisense oligonucleotides for novel targets, Q-RT-PCR and microarrays for expression analysis.
- Identification and characterization of novel mechanisms for antisense oligonucleotides. Includes computational genomics to identify mRNA variants, alteration of RNA processing, evaluation of siRNA and miRNA mechanisms.
- Biophysical and biochemical evaluation of novel antisense oligonucleotides. Includes: thermodynamics and kinetics of hybridization to oligonucleotide and large structured targets, evaluation of biochemical properties novel

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oligonucleotides, characterization of antisense activity in cell assays, protein-oligonucleotide binding.

- Characterization and screening of combinatorial libraries. Includes: theoretical and experimental evaluation of strategies for deconvolution, high throughput screening of combinatorial libraries, bacterial RNA-protein interactions.
- Development of non-radioactive DNA oligonucleotide probe based tests for detection of infectious and genetic diseases. Experience in: isolation of DNA from clinical samples, probe design, hybridization optimization, assay simplification, process validation. Includes: development of FDA cleared clinical tests for the direct detection of rotavirus or *Campylobacter* in stool, development of colony filter tests for bacterial identification and *in situ* hybridization tests for detection of virus in fixed tissues, cultured cells or patient specimens.
- Postdoctoral research with Douglas H. Turner on nucleic acid structure and dynamics. Experience in: chemical and enzymatic synthesis of oligonucleotides (deoxy- and ribo-), hybridization thermodynamics and kinetics, development of a laser temperature jump apparatus, NMR spectroscopy, computer programming and interfacing to laboratory instruments.
- Postdoctoral research with Irving M. Klotz and Richard P. Van Duyne on resonance Raman spectroscopy of DNA-mutagen interactions and resonance Raman spectroscopy of hemerythrin. Experience in: protein isolation, laser Raman spectroscopy.
- Graduate research on the solution conformation of transfer RNA.
Thesis title: Studies of Nucleic Acid Chemistry:
Part I. The Solution Structure of Yeast Initiator Transfer RNA Studied by Oligonucleotide Binding
Part II. A Chemical Model of Mutagenesis
Experience in: isolation of tRNA, oligoribonucleotide synthesis, oligonucleotide hybridization, NMR spectroscopy.
Research Advisor: Ignacio Tinoco Jr.

Molecular
Biosystems Inc.
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Rochester
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University of
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PUBLICATIONS

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Barry M. Casper, Susan M. Freier and David Van Atta, "Time Evolution in Statistical Mechanics", *American Journal of Physics* **41**, 1358-1360 (1973).

Susan M. Freier and Ignacio Tinoco, Jr. "The Binding of Complementary Oligoribonucleotides to Yeast Initiator Transfer RNA", *Biochemistry* **14**, 3310-3314 (1975).

Joseph A. Walder, Roxanne Y. Walder, Michael J. Heller, Susan M. Freier, Robert L. Letsinger and Irving M. Klotz, "Complementary Carrier Peptide Synthesis: General Strategy and Implications for Prebiotic Origin of Peptide Synthesis", *Proc. Nat. Acad. Sci. U.S.A.* **76**, 51-55 (1979).

Susan M. Freier, Lori L. Duff, Richard P. Van Duyne and Irving M. Klotz, "Resonance Raman Studies of a Sulfide Complex of Methemerythrin", *Biochemistry* **24**, 5372-5377 (1979).

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Timothy A. Vickers, Michael C. Griffith, Kanda Ramasamy, Lisa M. Risen and Susan M. Freier, "Inhibition of NF-  B specific transcriptional activation by PNA strand invasion", *Nucleic Acids Res.*, **23**, 3003-3008 (1995).

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Elena A. Lesnik and Susan M. Freier, "Relative thermodynamic stability of DNA, RNA and DNA:RNA hybrid duplexes, relationship with base composition and structure", *Biochemistry*, **34**, 10807-10815 (1995).

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Richard H. Griffey, Brett P. Monia, Lendall L. Cummins, Susan M. Freier, Michael J. Greig, Charles J. Guinasso, Elena Lesnik, Sherilynn M. Manalili, Venkatraman Mohan, Steven Owens, Bruce R. Ross, Henri Sasmor, Ed Wanciewicz, Kurt Weiler, Patrick D. Wheeler and P. Dan Cook, "2'-O-Aminopropyl Ribonucleotides: A Zwitterionic Modification that Enhances the Exonucleos Resistance and Biological Activity of Antisense Oligonucleotides", *J. Med. Chem.*, **39**, 5100-5109.

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Muthiah Manoharan, Laura K. Andrade, Venatraman, Mohan, Susan M. Freier and P. Dan Cook, "Oligonucleotide Conjugates Derived from an Electrophilic Site: Conjugation to Baseless Carbohydrate Residue. Synthesis, Hybridization and Modeling Studies", *Nucleosides and Nucleotides*, **16**, 1741-1744 (1997)

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